PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	COVID-19 vaccine hesitancy among undocumented migrants during the early phase of the vaccination campaign: a multi-centric cross-sectional study
AUTHORS	Page, Kathleen; Genovese, Eleonora; Franchi, Matteo; Cella, Silvano; Fiorini, Guianfrancesco; Tlili, Rim; Salazar, Sebastian; Duvoisin, Aline; Cailhol, Johann; Jackson, Yves

VERSION 1 – REVIEW

REVIEWER	Saudamini Dabak Health Intervention and Technology Assessment Program
REVIEW RETURNED	18-Sep-2021

GENERAL COMMENTS	Comments to the authors Title: Undocumented migrants' access to and demand for COVID-19 vaccination during the early phase of the vaccination campaign in four high-income countries Thank you for the opportunity to review this interesting paper. Vaccination of undocumented migrants is a topic that is important and needs to be addressed globally. In this regard, we have a few comments for the consideration of the authors: • Methods o It would be helpful for the authors to explain the choice of the three study sites – was this on account of the availability/access of the authors? o In terms of the objectives, is the main objective to understand vaccine hesitancy among undocumented workers or perceptions of vaccines among undocumented migrants? This may have implications on how the results on vaccine demand are presented. o In determining the odds ratios (Tables 5,6), what type of regression analysis was conducted? In what way were the results adjusted (for missing values?). Please clarify. o The presentations of results could be clarified – for example in Table 1, the "total" number for Milan is incomplete (N=126?) and the number in the fourth row for "missing" for Milan is not provided. It is also not clear what the missing numbers refer to. o Also, it would be helpful to add standard notation on significance to the tables (star signs against significant p-values). • Results o Could the authors please clarify what the model has been adjusted for in Table 6? o It is not clear that combining the results across the three sites offers insights across specific migrant groups, given the contextual features of where the respondents are located. There may be a higher proportion of respondents belonging to a certain background in one site than in another, which may not be generalisable. Moreover, the sample of respondents varies substantially from one

	site to another. • Discussion o The limitation on account of bias in sampling may require further enquiry, given that the respondents were those at the clinic, who may display health-seeking behavior, thus overestimating their expected access to vaccines. o On hesitancy, it would be helpful to elaborate further on perceived versus actual risk of getting the disease. The latter could be determined by using a proxy estimate such as occupation (which can be indicative of the level of risk of exposure to COVID-19). o Further, in terms of acceptability of vaccines, could the authors comment on whether respondents could assess the risks and benefits of COVID-19 vaccines? Additionally, the discussion ought to consider/control for the level of infection in the country at the time of the survey, which may impact the level of perceived risk of infection (and therefore willingness to get vaccinated). o It may be useful to comment on the structural barriers to accessing vaccines for undocumented migrants. From the survey results, language barriers are mentioned, and it is interesting that while most have indicated the lack of a national health insurance card, a fewer number indicates the lack of eligibility being an issue. Furthermore, it is surprising that most respondents would prefer to get vaccinated at hospitals rather than public health/community clinics (where they are completing this survey?); what could be the reason for this? o The results also have implications for policy recommendations, for example, whether governments focus on women in COVID-19 vaccinations strategies or is there a role for providing targeted information. It may be helpful to elaborate on this and potentially identify future areas for research. Thank you. Comments prepared by Saudamini Dabak, Manit Sittimart and Dr. Yot Teerawattananon

REVIEWER	Daniel La Parra University of Alicante, Department of Sociology
REVIEW RETURNED	09-Nov-2021

GENERAL COMMENTS	A descriptive paper about the self-perceived access to vaccination and vaccination demanda by undocumented migrants in four different cities at the early stages of the vaccination program. My main concern is about the analytical strategy. The authors decided to merge the data as if they would belong to the same population. For instance, in table 5, the data about Geneva are taken as the reference for the logistic regression analysis, but the populations they compare belong to different contexts and respond to diverse institutional practices (they were recruited from different facilities -mainly hospitals- in countries with a very different way of organising their health systems, especially in regard to undocumented migrants), the final selected sample could differ from the others not only because of the variables they are comparing, but also because of sampling selection and participation bias (related with the institutional structure and other reasons - immigrants living conditions, perceived discrimination, institutional racism, and so on). The migration systems in the Americas and Europe are very different, but we also find important differences between countries in Europe, and among different locations within a country, the consequence of this would produce differentiated sample

	composition in every location in terms of places of origin, time of residence, level of access, age, gender and other key sociodemographic variables are very diverse. The consequence of all this is that the populations can not be directly compared. This affects different parts of the manuscript, but mainly the results section. For instance, the p value column in tables 1 and 2; tables 5 and 6 (in my view, stratified analysis for every location would be more suitable). The previous comment does not affect the interest of the paper, which is mainly descriptive about statistically invisible populations in different countries. The absence of other sources of information about these populations has been solved by producing primary data by the research team which provide a quite unique source of information about these groups of the population. Minor comments: 1) There is a growing literature about the role of trust in reducing vaccination hesitancy (trust in the healthcare professionals and politicians). I would mention this component in the discussion. Level of trust may be reduced, a) if undocumented migrants experience discrimination from health professionals, b)they do not have direct access to healthcare, and c) they are targeted by some politicians. 2) I suggest avoiding the term "other vulnerable populations". Immigrants are more resilient than vulnerable. We can say there are living in vulnerable conditions. I would prefer to talk about discriminated populations. 3) Due to the sampling strategies, I would recommend to remind in every comparison among locations that they can be misperceived by the sampling strategy. 4) There is I at the end of the "setting description" in the abstract. 5) To state response rates in the four samples.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Methods
- It would be helpful for the authors to explain the choice of the three study sites – was this on account of the availability/access of the authors?
The study partner sites belong to an informal network of institutions active in the provision of medical care to undocumented migrants in Europe and the US. This has been added in the Setting sub-section.

- In terms of the objectives, is the main objective to understand vaccine hesitancy among undocumented workers or perceptions of vaccines among undocumented migrants? This may have implications on how the results on vaccine demand are presented.
We thank the reviewer for their demand of clarification. Indeed, the main focus was to understand vaccine hesitancy in this group by exploring various underlying domains including perception of accessibility, safety, etc. We clarified this point in the title (COVID-19 vaccine hesitancy among

undocumented migrants during the early phase of the vaccination campaign: a multi-centric cross-sectional study), in the introduction, methods and discussion sections.

- In determining the odds ratios (Tables 5,6), what type of regression analysis was conducted? In what way were the results adjusted (for missing values?). Please clarify.
Odds ratios were estimated through multivariate logistic regression models, which were mutually adjusted by factors reported, respectively, in Table 5 and Table 6. Missing values were imputed by using a multiple imputation approach. Briefly, multiple imputation is a bayesian method that allows to take into account incomplete cases (i.e. observations with any missing data) with a two-step approach. First, this method creates multiple imputed datasets, in which missing values are replaced by imputed values. These are sampled from their predictive distribution based on the observed data. The imputation procedure fully accounts for the uncertainty in predicting the missing values by conferring appropriate variability into the multiple imputed values. Second, standard statistical methods are used to fit the model of interest to each of the imputed datasets. Estimates associated to each of the imputed datasets differ because of the variation introduced in the imputation of the missing values (stage 1), and they are, then, average together to give overall estimated associations. Valid inferences are obtained because they are based on the average of the distribution of the missing data given the observed data [Sterne J.A. et al. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. BMJ,338:b2393,2009.]. We complemented the section accordingly.

- The presentations of results could be clarified – for example in Table 1, the “total” number for Milan is incomplete (N=126?) and the number in the fourth row for “missing” for Milan is not provided. It is also not clear what the missing numbers refer to.
We thank the reviewers for their careful revision and apologize for the typing errors that have been corrected. “Missing” refer to missing values for each variables, which has been corrected in the tables.

- Also, it would be helpful to add standard notation on significance to the tables (star signs against significant p-values).
We did not add this kind of notation in the tables as it is recommended by this Journal. We would happily do so if the Editor confirms it is necessary and acceptable.

Results
- Could the authors please clarify what the model has been adjusted for in Table 6?
Odds ratios were mutually adjusted by all the covariates reported in Table 6, including demographic characteristics (i.e. sex, age, region of origin and study site), clinical characteristics (i.e. presence of at least one comorbidity and COVID-19 infection) and factors related to self-perceived risk of COVID-19, accessibility to COVID-19 vaccinations, positive view of vaccination and use of media for accessing information about COVID-19.

- It is not clear that combining the results across the three sites offers insights across specific migrant groups, given the contextual features of where the respondents are located. There may be a higher proportion of respondents belonging to a certain background in one site than in another, which may not be generalisable. Moreover, the sample of respondents varies substantially from one site to another.
The reviewer is correct. In order to better reflect differences across sites, we provided regression analysis stratified by site in an appendix to the main document and discussed key results in the result section.

Discussion

- The limitation on account of bias in sampling may require further enquiry, given that the respondents were those at the clinic, who may display health-seeking behavior, thus overestimating their expected access to vaccines.
We thank the reviewers to raise this important point and we agree with their view. We added a comment about it and the need to challenge our findings by conducting similar surveys outside the healthcare setting (paragraph 5, 2nd sentence).

- On hesitancy, it would be helpful to elaborate further on perceived versus actual risk of getting the disease. The latter could be determined by using a proxy estimate such as occupation (which can be indicative of the level of risk of exposure to COVID-19).
The reviewers are correct. We try to respond to that point in the after next query taking into account the epidemiological situation and the public debate about the use of a new vaccine technology based on mRNA (see below). In addition we discussed a possible correlation between the reported fear of severe disease with age and multimorbidity as factors underlying the perceived risk (paragraph 3 – end).

- Further, in terms of acceptability of vaccines, could the authors comment on whether respondents could assess the risks and benefits of COVID-19 vaccines?
We developed our questionnaire relying on WHO, UNICEF and ECDC tools designed to investigate the factors underlying vaccine hesitancy. We tried to investigate the key domains which may influence participants' assessment of the risks-benefits balance of the COVID-19 vaccination taking into account specific circumstances faced by migrants but we cannot claim that our findings reflect the whole range of factors at stake. We added a line about this in the limitation section (last sentence).

- Additionally, the discussion ought to consider/control for the level of infection in the country at the time of the survey, which may impact the level of perceived risk of infection (and therefore willingness to get vaccinated).
We thank the reviewers for this important point. As a preliminary information, we added a description of the epidemiological situation and the vaccines available in each study site at the time of the survey. In the discussion, we develop the possible influence of these elements highlighting the potential effect of a lesser epidemiological pressure and of fears related to new mRNA technologies on how participants assessed risks and benefits of being vaccinated.

- It may be useful to comment on the structural barriers to accessing vaccines for undocumented migrants. From the survey results, language barriers are mentioned, and it is interesting that while most have indicated the lack of a national health insurance card, a fewer number indicates the lack of eligibility being an issue. Furthermore, it is surprising that most respondents would prefer to get vaccinated at hospitals rather than public health/community clinics (where they are completing this survey?); what could be the reason for this?
The reviewers raise important points. We have added a discussion about: a) the hypothesis of internalization of restriction to the access to essential services such as those provided by the healthcare system by undocumented migrants underlying the notion that services to the general population are not accessible as theorized by Chauvin and Garcia Mascarena; and b) the preference for Hospitals perceived as safer in regards to the appreciation of vaccines potentially being dangerous and in regards to the security of one's personal data (see the hypothesis of firewall, PICUM 2020) as compared to private or smaller clinics.

- The results also have implications for policy recommendations, for example, whether governments focus on women in COVID-19 vaccinations strategies or is there a role for providing targeted information. It may be helpful to elaborate on this and potentially identify future areas for research.
We agree with the reviewers and added discussion about the potential for targeted information to younger migrants, men and those with low clinical risk profiles. We proposed a set of

recommendations for future areas of research including long-term monitoring of hesitancy, vaccine promotion based on social media and community ressources, etc. (end of last paragraph).

Reviewer 2

- My main concern is about the analytical strategy. The authors decided to merge the data as if they would belong to the same population. For instance, in table 5, the data about Geneva are taken as the reference for the logistic regression analysis, but the populations they compare belong to different contexts and respond to diverse institutional practices (they were recruited from different facilities - mainly hospitals- in countries with a very different way of organising their health systems, especially in regard to undocumented migrants), the final selected sample could differ from the others not only because of the variables they are comparing, but also because of sampling selection and participation bias (related with the institutional structure and other reasons - immigrants living conditions, perceived discrimination, institutional racism, and so on). The migration systems in the Americas and Europe are very different, but we also find important differences between countries in Europe, and among different locations within a country, the consequence of this would produce differentiated sample composition in every location in terms of places of origin, time of residence, level of access, age, gender and other key sociodemographic variables are very diverse. The consequence of all this is that the populations can not be directly compared. This affects different parts of the manuscript, but mainly the results section. For instance, the p value column in tables 1 and 2; tables 5 and 6 (in my view, stratified analysis for every location would be more suitable).

The reviewer is correct about the fact that populations, settings and local circumstances about COVID-19 vary across study sites. We had to balance decisions about how to best merge and summarize our data while taking these differences into account. Considering also reviewer 1 query, we have added the results of the regression analysis for the two endpoints stratified by study site as an appendix to better highlight specificities pertaining to each location. We summarized the main results in the results section and highlighted the need to adapt to local circumstances in the discussion.

Minor comments:

- There is a growing literature about the role of trust in reducing vaccination hesitancy (trust in the healthcare professionals and politicians). I would mention this component in the discussion. Level of trust may be reduced, a) if undocumented migrants experience discrimination from health professionals, b) they do not have direct access to healthcare, and c) they are targeted by some politicians.

We agree with the reviewer that trust building is a key strategic element in any health intervention targeting this group at high risk of discrimination and stigmatization. We strengthened that point in the last paragraph of the discussion section and added the reference of Deal A. et. J Migr Health. 2021;4:100050 that specifically covers this point.

- I suggest avoiding the term "other vulnerable populations". Immigrants are more resilient than vulnerable. We can say there are living in vulnerable conditions. I would prefer to talk about discriminated populations.

The reviewer is right, using socially disadvantaged groups is more appropriate. We brought this modification in the manuscript.

- Due to the sampling strategies, I would recommend to remind in every comparison among locations that they can be misperceived by the sampling strategy.

We inserted a comment on this topic in the limitation paragraph of the discussion section: “Moreover, differences in sampling strategies and participants sociodemographic characteristics imply limitations in comparability among locations.”

- There is I at the end of the "setting description" in the abstract.
Thank you for the notification. We deleted it.

- To state response rates in the four samples.
The questionnaire was implemented as part of regular operations during the study period and we did not precisely measure the response rate which we regret. In all four settings, investigators and health professionals mentioned that it almost all participants completed it.

VERSION 2 – REVIEW

REVIEWER	Saudamini Dabak Health Intervention and Technology Assessment Program
REVIEW RETURNED	16-Jan-2022

GENERAL COMMENTS	Thank you for addressing the comments raised earlier. Minor comments on the revision: 1) On the targeting policies in the discussion, consider unpacking the higher odds of uptake among women; they too may be able to champion use of vaccination for themselves and their families. That is to say, they may be strong partners for any initiative increasing vaccination rates. As indicated in the appendix, one may note that gender is only significant in univariate analysis and also found to be significant in only two of four locations. 2) On the results reported in the Appendix, is there any reason why multi-variate analysis was not conducted for Milan on Positive views on Immunization (COVID-19). 3) For Milan and Baltimore, could you confirm that the variable "Positive views on Immunization (general)" was dropped due to collinearity? 4) It may be helpful for the authors to do a proof-reading of the paper.

REVIEWER	Daniel La Parra University of Alicante, Department of Sociology
REVIEW RETURNED	30-Dec-2021

GENERAL COMMENTS	The authors have addressed all the comments raised by the reviewers. I do not have additional comments.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

1) On the targeting policies in the discussion, consider unpacking the higher odds of uptake among women; they too may be able to champion use of vaccination for themselves and their families. That is to say, they may be strong partners for any initiative increasing vaccination rates. As indicated in the appendix, one may note that gender is only significant in univariate analysis and also found to be significant in only two of four locations.

Authors response :

The reviewer is correct. We believe we had already stressed this point in the discussion in two differents paragraphs:

1. In the second paragraph discussing the results, we wote

"In our study, women were more likely to endorse access than men. This could be related to increased familiarity with the vaccination programs and overall health system through the use of reproductive health services and as traditional caregivers for children."

2. In the last paragraph, we implied the importance of gender indirectly by stressing the specifi need to direct information on men: "Information and promotion of vaccination should particularly focus on men, younger migrants and those with low clinical risks highlighting both individual and collective benefits and reassuring about vaccines safety". In order to make the role of women more explicit, we added :“Women should be seen as key partners in trust-building initiatives promoting vaccination.“

2) On the results reported in the Appendix, is there any reason why multi-variate analysis was not conducted for Milan on Positive views on Immunization (COVID-19).

The multivariate analysis failed to estimate the odds ratio, due to the low frequencies in some cells. Indeed, also in the univariate analysis, the estimate of the odds ratio was rather inaccurate, with a wide confidence interval.

We added, at the bottom of each table in the new version of the Appendix, a note explaining that some odds ratio are not estimable, due to empty cells or cells with low frequencies.

3) For Milan and Baltimore, could you confirm that the variable "Positive views on Immunization (general)" was dropped due to collinearity?

Yes, for both Milan and Baltimore, the logistic model failed to estimate the odds ratio because in all individuals with positive views on immunization (general) the demand for COVID-19 vaccination (outcome 2) was 100%.

We added, at the bottom of each table in the new version of the Appendix, a note

explaining that some odds ratio are not estimable, due to empty cells or cells with low frequencies.

4) It may be helpful for the authors to do a proof-reading of the paper.

Thank you for the suggestion. We proof-read the manuscript to remove all mistakes.